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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,328	04/13/2007	Makoto Sawada	084335-0201	9146

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
BALLARD, KIMBERLY	
ART UNIT	PAPER NUMBER
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,328	SAWADA, MAKOTO	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *13,14,24 and 26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 11* is/are rejected.

7)☒ Claim(s) *7-10,12,15-23 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :02/07/2006; 07/06/2006; 08/21/2007; 05/28/2008; 11/25/2008; 05/27/2009.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-12, 15-23 and 25, drawn to a polypeptide having brain-localizing activity, pharmaceutical compositions thereof, first recited method of production and first recited method of use, in the reply filed on April 24, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-30 are pending in the current application.

3. Claims 13, 14, 24, and 26-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 24, 2009.

Accordingly, claims **1-12, 15-23** and **25** are under examination in the present office action.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on the following dates have been considered: February 7, 2006; July 6, 2006; August 21, 2007; May 28, 2008; November 25, 2008; and May 27, 2009.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

6. Claims 7-10, 12, 15-23 and 25 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-6 and 11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Specifically, the claims are directed to a polypeptide having brain-localizing activity. It is noted that the limitations reciting cyclic peptides, particular amino acid residues within particular regions of the polypeptide, or else substitutions, and/or deletions or additions to the amino acid sequence of any of SEQ ID NOs: 1-12 do not serve to distinguish the claimed polypeptides from those which occur in nature, such as a cyclic peptide or peptide

variant of SEQ ID NOs: 1-12 that are still in a living being. It is noted that inclusion of the phrase “isolated” would overcome this rejection.

Claim Rejections - 35 USC § 112, second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4 and 6 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-4 and 6, the phrase in parentheses “(K or R)” renders the claim indefinite because it is unclear whether the limitations within the parentheses are part of the claimed invention. The instant situation is akin to use of the phrase "such as" in a claim. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112, first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-6 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

All of the claims under examination require that the claimed polypeptide has brain-localizing activity. The specification at pages 7-11 discloses that such polypeptides can vary in length and in composition so long as the polypeptide comprises a motif sequence consisting of 4 amino acids, which motif sequence (Sequence 1, 2, or 3) is disclosed as X_1-(R or K)-X_3-X_4 or X_4-X_3-(R or K)-X_1, wherein X_3 denotes an arbitrary amino acid and X_1 and X_4 are defined amino acid residues selected from a group of specific amino acids. The specification discloses 12 species within the claimed genus; specifically, the polypeptides having the amino acid sequences of SEQ ID NOs: 1-12.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Applicants are directed to the recently-published guidelines on interpretation of the written description requirement, available on the internet at: http://www.uspto.gov/web/menu/written.pdf . See in particular Examples 9 and 10, drawn to protein variants including those with recited functions.

The recitation of a polypeptide having 10% or more of the polypeptide comprised of basic amino acid residues K or R (or at least one or more of the residues in the cyclic

region are K or R), or a polypeptide in which 80% or more of the remaining amino acids in the cyclic region are comprises of G, A, V, L, S, T, P, Q, H, or N, or a polypeptide comprising a sequence with one or several amino acid additions, substitutions, or deletions in the amino acid sequence of any of SEQ ID NOs: 1-12, represents a partial structure. That is, the polypeptide's structure can vary substantially within the above given claimed recitations, even given the disclosure of a polypeptide comprising the above-disclosed sequence motif. In other words, the specification does not provide sufficient guidance as to which of the multitude of amino acid residues within claimed polypeptides (which are not claimed as requiring the disclosed motif) can be varied while still retaining brain-localizing activity. Further, there is no art-recognized correlation between any particular motif and brain-localizing activity, Based on which those of ordinary skill in the art could predict which amino acids can vary from SEQ ID NOs: 1-12 without losing the brain-localizing activity. Consequently, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NOs: 1-12, the skilled artisan cannot envision the detailed chemical structure of the encompassed claimed polypeptides (if any) which have the activity of brain-localization without further testing, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 (BPAI 1993). In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NOs: 1-12, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-6 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 5 of copending Application No. 12/064,691 (hereinafter the '691 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '691 application contains claims directed to a brain-localizing cell that expresses the instantly claimed brain-localizing polypeptide. The claimed cell of the '691 application therefore comprises the presently claimed brain-localizing polypeptide, such as a polypeptide comprising the motif of claim 5 or a polypeptide having the amino acid sequence of any of SEQ ID NOs: 1-12, and would render such polypeptides obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1-6 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Pasqualini & Ruoslahti (*Nature*, 1996; 380(6572):364-366; listed on IDS filed 02/07/2006).

Pasqualini & Ruoslahti teach peptides with brain localizing activity which were determined through use of phage display peptide libraries. One of these peptides, CLSSRLDAC, has a peptide sequence comprised of 10% or more (in this case, 11.1%) of basic amino acid residues K or R (in this case R, as in CLSS**R**LDAC), thus meeting recited limitations of instant claims 1 and 2. Pasqualini & Ruoslahti also disclose that the peptide CLSSRLDAC was synthesized as a cyclic peptide, which gave it slightly better brain localizing activity (see paragraph spanning pp. 365-366), which would address recited limitations of claims 2-4 regarding a cyclic peptide. In addition to the CLSSRLDAC peptide comprising one basic amino acid residue, R, 83.3% of the remaining amino acid residues in the cyclic region are L, S or A, thus addressing a recited limitation of instant claim 4. With respect to claims 5 and 6, the peptide CL<u>SSRL</u>DAC comprises the motif sequence of X_4-X_3-(R or K)-X_1, wherein X_4 is S, X_3 is S, and X_1 is L, as recited in claim 5 (motif sequence is underlined).

Pasqualini & Ruoslahti also teach brain-localizing peptides comprising the motif of CVLRGGRC (see 2nd column on p. 364). A peptide comprising this disclosed motif would thus meet a limitation of instant claim 11, which recites a polypeptide having brain-localizing activity, and comprising an amino acid sequence with one or several amino acid additions, deletions, or substitutions in the amino acid sequence of any one of SEQ ID NOs: 1-12. In this case, the CVLRGGRC peptide motif is similar to the instantly recited SEQ ID NO: 5 (CVLRHLQQC) wherein 3 amino acids have been substituted (e.g., GGR for HLQ) and one amino acid has been deleted (e.g., Q). Moreover, because there is no limit to the number of additions, deletions, or substitutions to the polypeptide recited in (c) of instant claim 11 so long as the peptide retains brain-localizing activity, any one of the several brain-localizing peptides disclosed by Pasqualini & Ruoslahti would meet the limitations of the claim. As such, the teachings of Pasqualini & Ruoslahti clearly anticipate the invention of present claims 1-6 and 11.

17. Claims 1-6 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2007/0254316 A1 by Rodriguez et al. (published November 1, 2007; filed August 5, 2003).

Rodriguez et al. disclose peptide compounds and pharmaceutical compositions thereof, which bind to the extracellular portion of the human prostate specific membrane antigen (PSMA). One of these peptides, SEQ ID NO: 85, is identical to the instantly

claimed polypeptide comprising the amino acid sequence of SEQ ID NO: 2. See, for example, results in SCORE and the following sequence alignment:

```
PN   WO2006028429-A2.
XX
PD   16-MAR-2006.
XX
PF   05-AUG-2003; 2003WO-US024660.
XX
PR   05-AUG-2002; 2002US-0401151P.
PR   20-DEC-2002; 2002US-0435140P.
XX
PA   (UYJO ) UNIV JOHNS HOPKINS.
XX
PI   Rodriguez R,  Lupold SE;
XX
PT   New peptide compound, which binds to prostate specific membrane antigen,
PT   useful for diagnosing and treating prostate cancer.
XX
PS   Claim 1; SEQ ID NO 85; 47pp; English.
XX
SQ   Sequence 9 AA;

  Query Match             100.0%;  Score 51;  DB 1;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 3.9e+06;
  Matches  9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CSLNTRSQC 9
              |||||||||
Db          1 CSLNTRSQC 9
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Note that above, Qy (query) = the instant SEQ ID NO: 2 and Db (database) = Rodriguez's SEQ ID NO: 85. The peptide of SEQ ID NO: 85 therefore has 10% or more of the peptide comprised of basic amino acids K or R. Rodriguez et al. also disclose that the peptide of SEQ ID NO: 85 may be a cyclic peptide (see paragraphs [0029-0030] and claim 33 on page 36), thus addressing recited limitations of claims 2-4. Additionally, all of the remaining amino acid residues in the cyclic region of SEQ ID NO: 85 are S, L, D, T, or Q, which addresses a limitation of instant claim 4. Because the disclosed peptide of SEQ ID NO: 85 is identical to the instantly recited SEQ ID NO: 2, it would inherently

possess the property of having brain-localizing activity. A chemical composition and its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)), as are their processes and yields (*In re Von Schickh*, 362 F.2d 821, 150 USPQ 300 (CCPA 1966)). Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Accordingly, the disclosure of the Rodriguez et al. document anticipates instant claims 1-6 and 11.

Conclusion

18. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 9 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kimberly Ballard
Art Unit 1649

/Elizabeth C. Kemmerer/
Elizabeth C. Kemmerer, Ph.D.
Primary Examiner, Art Unit 1646